



Are Medications Involved in Vision and Intracranial Pressure Changes Seen in Spaceflight?

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INTRODUCTION

Some crewmembers have experienced changes in their vision after long-duration spaceflight on the ISS. These impairments include visual performance decrements, development of cotton-wool spots or choroidal folds, optic-disc edema, optic nerve sheath distention, and/or posterior globe flattening with varying degrees of severity and permanence. These changes are now used to define the visual impairment/intracranial pressure (VIIP) syndrome. It is known that many medications can have side effects that are similar to VIIP symptoms. Some medications raise blood pressure, which can affect intracranial pressure. Many medications that act in the central nervous system can affect intracranial pressures and/or vision. About 40% of the medications in the ISS kit are known to cause side effects involving changes in blood pressure, intracranial pressure and/or vision. For this reason, we have begun an investigation of the potential relationship between ISS medications and their risk of causing or exacerbating VIIP-like symptoms.

METHODS

The medical literature indicates that pain relievers, especially non-steroidal anti-inflammatory (NSAID) medication (like ibuprofen) and glucocorticoids (like dexamethasone) were among the most likely candidate medications, and have the focus of initial queries for this study. Two different data sources were examined.

Data from the general population: The Food and Drug Administration (FDA) maintains a system for collecting suspected medication adverse events in their Adverse Event Reporting System (AER). Patients and medical professionals may enter data regarding suspected events and these unconfirmed raw data are available for public download. In this study, we downloaded 3 years of data representing over 1 million suspected medication-related adverse events from January 2009 – December 2011. To better model the astronaut corps, cases involving individuals younger than 25 or older than 65 were removed from our analysis. Similarly, cases involving cancer, multiple sclerosis or other serious and chronic conditions were removed. Medications used in cases associated with VIIP-like symptoms were examined.

# AERs with VIIP-like symptoms	
Ibuprofen	117
Aspirin	180
Acetaminophen	110
Hydrocortisone	8
Dexamethasone	39
Prednisone	192
Pseudoephedrine	12
Promethazine	14
Benadryl	31
Dexedrine	4

Table 1. Total occurrences of VIIP-like symptoms associated with use of each listed medication in the general population from 2009 - 2012. Data are from the FDA AERs and thus, indicate occurrence of symptoms correlated with use of each medication; causality has not been confirmed. Furthermore, **these data do not permit an estimate of occurrence rate**, because there is no measure of total medication use or medication use without adverse events.

PRELIMINARY RESULTS

Figure 1. Occurrence of VIIP-like Symptoms With Suspected Link to Medication Use in the General Population

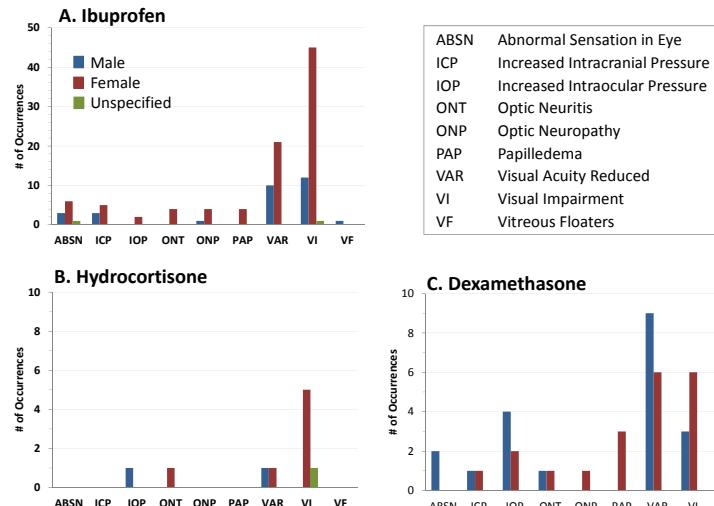


Figure 1. Possible gender effects of the listed symptoms associated with medication use in the general population. A. Ibuprofen; B. Hydrocortisone; C. Dexamethasone. Note that incidences are higher among females for ibuprofen, but higher in males for dexamethasone. While changes in visual acuity and visual impairment are reported during use of many medications, dexamethasone also had reports of IOP changes.

Figure 2. Occurrence of VIIP-like Symptoms With Suspected Link to Prednisone Use Among Different Age Groups in the General Population

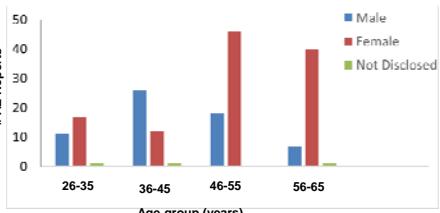


Figure 2. Occurrences of VIIP-like symptoms associated with prednisone use in the general population, grouped by subject age. Occurrence of prednisone-associated VIIP-like symptoms peaked in females from 36-45 years old and are higher in males at older ages.

Figure 3. VIIP-like Symptom Reports Are Reported by both Males and Females in their Middle Years

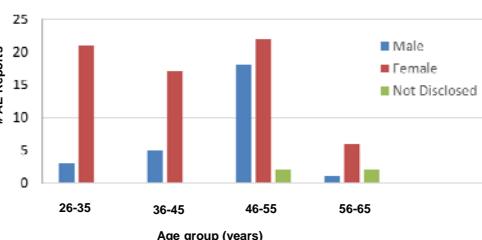


Figure 3. Reports of VIIP-like symptoms are associated with ibuprofen use in the general population. Results here are shown grouped by age range. Although, in general, more females report VIIP-like adverse events than males, reports are nearly equivalent in the 46-55 age group.

INTERIM CONCLUSIONS

The preliminary nature of this report must be taken into consideration when interpreting results. Crew cases are limited in number, and medication usage records lack details that would be helpful. For this reason, we are using the FDA AERs as an additional source of data. This is a extremely large data set, and while it includes persons who may not model the astronaut population, the sheer volume of data may highlight trends to examine in the crew data. FDA results are compromised by several factors, chiefly the lack of causal information regarding each report, but issues of incomplete data reporting and polypharmacy also play confounding roles.

However, certain trends may be noted:

- In the general population, use of several medications is associated with VIIP-like symptoms, with changes in visual acuity being the most common.
- In the general population, there may be gender trends with males over 46 years of age more likely to experience or report VIIP-like symptoms associated with prednisone use.
- In the general population, there may be a trend toward increased occurrences of VIIP-like symptoms with ibuprofen use by males from 36-65 years old; reports are higher for females from 26-55. For purposes of comparison, the average age of crewmembers at their first ISS mission is 46.6 years (range 37 – 54 years).

Further detailed examination of both data sets (general population and crew data) may permit more substantive correlations as this study progresses.

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